

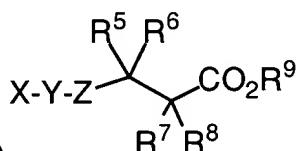
a¹ -- This application is a divisional of Serial No. 09/454,847, filed December 2, 1999, which is a divisional of Serial No. 09/212,082, filed December 15, 1998, which in turn is related to US provisional applications Serial No. 60/069,899, filed December 17, 1997; 60/083,209, filed April 27, 1998; 60/092,622, filed July 13, 1998; and 60/108,063, filed November 12, 1998; the contents of all of which are hereby incorporated by reference. --

IN THE CLAIMS:

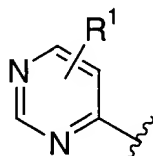
CANCEL Claims 1-40 ✓

ADD Claims 41-63

a² 41. A compound of the formula



wherein X is

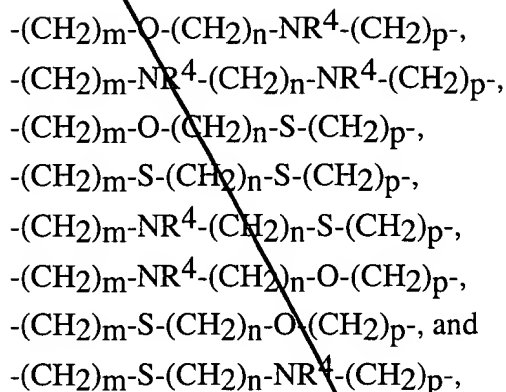


Y is selected from the group consisting of

- (CH₂)_m-,
- (CH₂)_m-O-(CH₂)_n-,
- (CH₂)_m-NR⁴-(CH₂)_n-,
- (CH₂)_m-S-(CH₂)_n-,
- (CH₂)_m-SO-(CH₂)_n-,
- (CH₂)_m-SO₂-(CH₂)_n-,
- (CH₂)_m-O-(CH₂)_n-O-(CH₂)_p-,

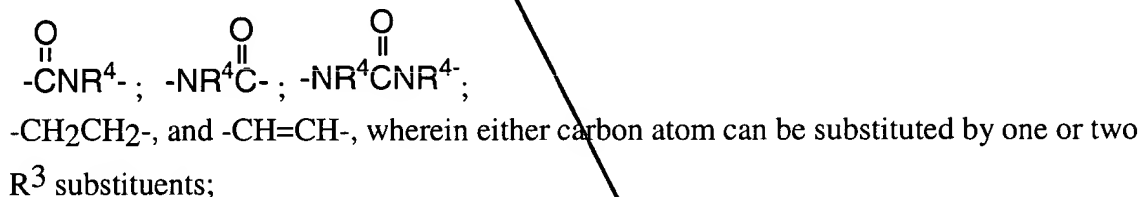
contd
a²

B¹
cont



wherein any methylene (CH₂) carbon atom in Y, other than in R⁴, can be substituted by one or two R³ substituents, with the proviso that when Y is $-(\text{CH}_2)_m-\text{NR}^4-(\text{CH}_2)_n-$ and $n = 1$, then the R³ substituent on the methylene carbon in $-(\text{CH}_2)_m-$ adjacent to the nitrogen cannot be oxo;

Z is selected from the group consisting of



R¹ and R² are each independently selected from the group consisting of

hydrogen, halogen, C₁₋₁₀ alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloheteroalkyl, C₃₋₈ cycloalkyl C₁₋₆ alkyl, C₃₋₈ cycloheteroalkyl C₁₋₆ alkyl, aryl, aryl C₁₋₈ alkyl, amino, amino C₁₋₈ alkyl, C₁₋₃ acylamino, C₁₋₃ acylamino C₁₋₈ alkyl, (C₁₋₆ alkyl)pamino, (C₁₋₆ alkyl)pamino C₁₋₈ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkoxy C₁₋₆ alkyl, hydroxycarbonyl, hydroxycarbonyl C₁₋₆ alkyl, C₁₋₃ alkoxycarbonyl, C₁₋₃ alkoxycarbonyl C₁₋₆ alkyl, hydroxycarbonyl-C₁₋₆ alkyloxy, hydroxy, hydroxy C₁₋₆ alkyl, C₁₋₆ alkyloxy-C₁₋₆ alkyl, nitro, cyano, trifluoromethyl, trifluoromethoxy,

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contd.

a²

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Cont

trifluoroethoxy, C₁₋₈ alkyl-S(O)_p, (C₁₋₈alkyl)_paminocarbonyl,
C₁₋₈ alkyloxy-carbonylamino, (C₁₋₈ alkyl)_paminocarbonyloxy,
(aryl C₁₋₈ alkyl)_pamino, (aryl)_pamino, aryl C₁₋₈
alkylsulfonylamino, and C₁₋₈ alkylsulfonylamino;

or two R¹ substituents, when on the same carbon atom, are taken together with the carbon
atom to which they are attached to form a carbonyl group;

each R³ is independently selected from the group consisting of

hydrogen,

aryl,

C₁₋₁₀ alkyl,

aryl-(CH₂)_r-O-(CH₂)_s-,

aryl-(CH₂)_r-S(O)_p-(CH₂)_s-,

aryl-(CH₂)_r-C(O)-(CH₂)_s-,

aryl-(CH₂)_r-C(O)-N(R⁴)-(CH₂)_s-,

aryl-(CH₂)_r-N(R⁴)-C(O)-(CH₂)_s-,

aryl-(CH₂)_r-N(R⁴)-(CH₂)_s-,

halogen,

hydroxyl,

oxo,

trifluoromethyl,

C₁₋₈ alkylcarbonylamino,

aryl C₁₋₅ alkoxy,

C₁₋₅ alkoxy-carbonyl,

(C₁₋₈ alkyl)_paminocarbonyl,

C₁₋₆ alkylcarbonyloxy,

C₃₋₈ cycloalkyl,

(C₁₋₆ alkyl)_pamino,

amino C₁₋₆ alkyl,

arylaminocarbonyl,

aryl C₁₋₅ alkylaminocarbonyl,

aminocarbonyl,

aminocarbonyl C₁₋₆ alkyl,
 hydroxycarbonyl,
 hydroxycarbonyl C₁₋₆ alkyl,
 HC≡C-(CH₂)_t-,
 C₁₋₆ alkyl-C≡C-(CH₂)_t-,
 C₃₋₇ cycloalkyl-C≡C-(CH₂)_t-,
 aryl-C≡C-(CH₂)_t-,
 C₁₋₆ alkylaryl-C≡C-(CH₂)_t-,
 CH₂=CH-(CH₂)_t-,
 C₁₋₆ alkyl-CH=CH-(CH₂)_t-,
 C₃₋₇ cycloalkyl-CH=CH-(CH₂)_t-,
 aryl-CH=CH-(CH₂)_t-,
 C₁₋₆ alkylaryl-CH=CH-(CH₂)_t-,
 C₁₋₆ alkyl-SO₂-(CH₂)_t-,
 C₁₋₆ alkylaryl-SO₂-(CH₂)_t-,
 C₁₋₆ alkoxy,
 aryl C₁₋₆ alkoxy,
 aryl C₁₋₆ alkyl,
 (C₁₋₆ alkyl)pamino C₁₋₆ alkyl,
 (aryl)pamino,
 (aryl)pamino C₁₋₆ alkyl,
 (aryl C₁₋₆ alkyl)pamino,
 (aryl C₁₋₆ alkyl)pamino C₁₋₆ alkyl,
 arylcarbonyloxy,
 aryl C₁₋₆ alkylcarbonyloxy,
 (C₁₋₆ alkyl)paminocarbonyloxy,
 C₁₋₈ alkylsulfonylamino,
 arylsulfonylamino,
 C₁₋₈ alkylsulfonylamino C₁₋₆ alkyl,
 arylsulfonylamino C₁₋₆ alkyl,
 aryl C₁₋₆ alkylsulfonylamino,
 aryl C₁₋₆ alkylsulfonylamino C₁₋₆ alkyl,

contd.

a²

B¹
cont

20009YDB

C₁₋₈ alkoxy-carbonylamino,
C₁₋₈ alkoxy-carbonylamino C₁₋₈ alkyl,
aryloxy-carbonylamino C₁₋₈ alkyl,
aryl C₁₋₈ alkoxy-carbonylamino,
aryl C₁₋₈ alkoxy-carbonylamino C₁₋₈ alkyl,
C₁₋₈ alkyl-carbonylamino,
C₁₋₈ alkyl-carbonylamino C₁₋₆ alkyl,
aryl-carbonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkyl-carbonylamino,
aryl C₁₋₆ alkyl-carbonylamino C₁₋₆ alkyl,
aminocarbonylamino C₁₋₆ alkyl,
(C₁₋₈ alkyl)paminocarbonylamino,
(C₁₋₈ alkyl)paminocarbonylamino C₁₋₆ alkyl,
(aryl)paminocarbonylamino C₁₋₆ alkyl,
(aryl C₁₋₈ alkyl)paminocarbonylamino,
(aryl C₁₋₈ alkyl)paminocarbonylamino C₁₋₆ alkyl,
aminosulfonylamino C₁₋₆ alkyl,
(C₁₋₈ alkyl)paminosulfonylamino,
(C₁₋₈ alkyl)paminosulfonylamino C₁₋₆ alkyl,
(aryl)paminosulfonylamino C₁₋₆ alkyl,
(aryl C₁₋₈ alkyl)paminosulfonylamino,
(aryl C₁₋₈ alkyl)paminosulfonylamino C₁₋₆ alkyl,
C₁₋₆ alkylsulfonyl,
C₁₋₆ alkylsulfonyl C₁₋₆ alkyl,
arylsulfonyl C₁₋₆ alkyl,
aryl C₁₋₆ alkylsulfonyl,
aryl C₁₋₆ alkylsulfonyl C₁₋₆ alkyl,
C₁₋₆ alkylcarbonyl,
C₁₋₆ alkylcarbonyl C₁₋₆ alkyl,
arylcarbonyl C₁₋₆ alkyl,
aryl C₁₋₆ alkylcarbonyl,
aryl C₁₋₆ alkylcarbonyl C₁₋₆ alkyl,

B1
cont

~~C1-6 alkylthiocarbonylamino,
C1-6 alkylthiocarbonylamino C1-6 alkyl,
arylthiocarbonylamino C1-6 alkyl,
aryl C1-6 alkylthiocarbonylamino,
aryl C1-6 alkylthiocarbonylamino C1-6 alkyl,
(C1-8 alkyl)paminocarbonyl C1-6 alkyl,
(aryl)paminocarbonyl C1-6 alkyl,
(aryl C1-8 alkyl)paminocarbonyl, and
(aryl C1-8 alkyl)paminocarbonyl C1-6 alkyl;~~

or two R³ substituents, when on the same carbon atom are taken together with the carbon atom to which they are attached to form a carbonyl group or a cyclopropyl group, wherein any of the alkyl groups of R³ are either unsubstituted or substituted with one to three R¹ substituents, and provided that each R³ is selected such that in the resultant compound the carbon atom or atoms to which R³ is attached is itself attached to no more than one heteroatom;

each R^4 is independently selected from the group consisting of

hydrogen,
aryl,
aminocarbonyl,
C₃₋₈ cycloalkyl,
amino C₁₋₆ alkyl,
(aryl)_paminocarbonyl,
(aryl C₁₋₅ alkyl)_paminocarbonyl,
hydroxycarbonyl C₁₋₆ alkyl,
C₁₋₈ alkyl,
aryl C₁₋₆ alkyl,
(C₁₋₆ alkyl)_pamino C₂₋₆ alkyl,
(aryl C₁₋₆ alkyl)_pamino C₂₋₆ alkyl,
C₁₋₈ alkylsulfonyl,
C₁₋₈ alkoxycarbonyl,
aryloxycarbonyl,
aryl C₁₋₈ alkoxycarbonyl,

[illegible]

contd.
a2

D1
cont

20009YDB

C₁₋₈ alkylcarbonyl,
arylcarbonyl,
aryl C₁₋₆ alkylcarbonyl,
(C₁₋₈ alkyl)_paminocarbonyl,
aminosulfonyl,
C₁₋₈ alkylaminosulfonyl,
(aryl)_paminosulfonyl,
(aryl C₁₋₈ alkyl)_paminosulfonyl,
arylsulfonyl,
arylC₁₋₆ alkylsulfonyl,
C₁₋₆ alkylthiocarbonyl,
arylthiocarbonyl, and
aryl C₁₋₆ alkylthiocarbonyl,

wherein any of the alkyl groups of R⁴ are either unsubstituted or substituted with one to three R¹ substituents;

R⁵ and R⁶ are each independently selected from the group consisting of

hydrogen,
C₁₋₁₀ alkyl,
aryl,
aryl-(CH₂)_r-O-(CH₂)_s-,
aryl-(CH₂)_r-S(O)_p-(CH₂)_s-,
aryl-(CH₂)_r-C(O)-(CH₂)_s-,
aryl-(CH₂)_r-C(O)-N(R⁴)-(CH₂)_s-,
aryl-(CH₂)_r-N(R⁴)-C(O)-(CH₂)_s-,
aryl-(CH₂)_r-N(R⁴)-(CH₂)_s-,
halogen,
hydroxyl,
C₁₋₈ alkylcarbonylamino,
aryl C₁₋₅ alkoxy,
C₁₋₅ alkoxycarbonyl,
(C₁₋₈ alkyl)_paminocarbonyl,

contd.
a²

B¹
cont

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C₁₋₆ alkylcarbonyloxy,
C₃₋₈ cycloalkyl,
(C₁₋₆ alkyl)pamino,
amino C₁₋₆ alkyl,
arylamino carbonyl,
aryl C₁₋₅ alkylamino carbonyl,
aminocarbonyl,
aminocarbonyl C₁₋₆ alkyl,
hydroxycarbonyl,
hydroxycarbonyl C₁₋₆ alkyl,
HC≡C-(CH₂)_t-,
C₁₋₆ alkyl-C≡C-(CH₂)_t-,
C₃₋₇ cycloalkyl-C≡C-(CH₂)_t-,
aryl-C≡C-(CH₂)_t-,
C₁₋₆ alkylaryl-C≡C-(CH₂)_t-,
CH₂=CH-(CH₂)_t-,
C₁₋₆ alkyl-CH=CH-(CH₂)_t-,
C₃₋₇ cycloalkyl-CH=CH-(CH₂)_t-,
aryl-CH=CH-(CH₂)_t-,
C₁₋₆ alkylaryl-CH=CH-(CH₂)_t-,
C₁₋₆ alkyl-SO₂-(CH₂)_t-,
C₁₋₆ alkylaryl-SO₂-(CH₂)_t-,
C₁₋₆ alkoxy,
aryl C₁₋₆ alkoxy,
aryl C₁₋₆ alkyl,
(C₁₋₆ alkyl)pamino C₁₋₆ alkyl,
(aryl)pamino,
(aryl)pamino C₁₋₆ alkyl,
(aryl C₁₋₆ alkyl)pamino,
(aryl C₁₋₆ alkyl)pamino C₁₋₆ alkyl,
arylcarbonyloxy,
aryl C₁₋₆ alkylcarbonyloxy,

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
0	0	1	4	9	16	25	36	49	64	81	100	121	144	169	196	225	256	289	324	361	400	441	484	529	576	625	676	729	784	841	900	961	1024	1089	1156	1225	1296	1369	1444	1521	1600	1681	1764	1849	1936	2025	2116	2209	2304	2401	2500	2601	2704	2809	2916	3025	3136	3249	3364	3481	3600	3721	3844	3969	4096	4225	4356	4489	4624	4761	4900	5041	5184	5329	5476	5625	5776	5929	6084	6241	6400	6561	6724	6889	7056	7225	7396	7569	7744	7921	8100	8281	8464	8649	8836	9025	9216	9409	9604	9801	10000

contd.

a²

B¹
cont

FOIA b 7 - D

aryl C₁₋₆ alkylsulfonyl,
aryl C₁₋₆ alkylsulfonyl C₁₋₆ alkyl,
C₁₋₆ alkylcarbonyl,
C₁₋₆ alkylcarbonyl C₁₋₆ alkyl,
arylcabonyl C₁₋₆ alkyl,
aryl C₁₋₆ alkylcarbonyl,
aryl C₁₋₆ alkylcarbonyl C₁₋₆ alkyl,
C₁₋₆ alkylthiocarbonylamino,
C₁₋₆ alkylthiocarbonylamino C₁₋₆ alkyl,
arylthiocarbonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkylthiocarbonylamino,
aryl C₁₋₆ alkylthiocarbonylamino C₁₋₆ alkyl,
(C₁₋₈ alkyl)_paminocarbonyl C₁₋₆ alkyl,
(aryl)_paminocarbonyl C₁₋₆ alkyl,
(aryl C₁₋₈ alkyl)_paminocarbonyl, and
(aryl C₁₋₈ alkyl)_paminocarbonyl C₁₋₆ alkyl;

or R⁵ and R⁶ are taken together with the carbon atom to which they are attached to form a carbonyl group,

wherein any of the alkyl groups of R⁵ or R⁶ are either unsubstituted or substituted with one to three R¹ substituents, and provided that each R⁵ and R⁶ are selected such that in the resultant compound the carbon atom to which R⁵ and R⁶ are attached is itself attached to no more than one heteroatom;

R⁷ and R⁸ are each independently selected from the group consisting of

hydrogen,
C₁₋₁₀ alkyl,
aryl,
aryl-(CH₂)_r-O-(CH₂)_s-,
aryl-(CH₂)_rS(O)_p-(CH₂)_s-,
aryl-(CH₂)_r-C(O)-(CH₂)_s-,
aryl-(CH₂)_r-C(O)-N(R⁴)-(CH₂)_s-,
aryl-(CH₂)_r-N(R⁴)-C(O)-(CH₂)_s-,

contd.

a²

B¹
cont

20009YDB

aryl-(CH₂)_t-N(R⁴)-(CH₂)_s-,
halogen,
hydroxyl,
C₁₋₈ alkylcarbonylamino,
aryl C₁₋₅ alkoxy,
C₁₋₅ alkoxy carbonyl,
(C₁₋₈ alkyl)_paminocarbonyl,
C₁₋₆ alkylcarbonyloxy,
C₃₋₈ cycloalkyl,
(C₁₋₆ alkyl)_pamino,
amino C₁₋₆ alkyl,
arylamino carbonyl,
aryl C₁₋₅ alkylaminocarbonyl,
aminocarbonyl,
aminocarbonyl C₁₋₆ alkyl,
hydroxycarbonyl,
hydroxycarbonyl C₁₋₆ alkyl,
HC≡C-(CH₂)_t-,
C₁₋₆ alkyl-C≡C-(CH₂)_t-,
C₃₋₇ cycloalkyl-C≡C-(CH₂)_t-,
aryl-C≡C-(CH₂)_t-,
C₁₋₆ alkylaryl-C≡C-(CH₂)_t-,
CH₂=CH-(CH₂)_t-,
C₁₋₆ alkyl-CH=CH-(CH₂)_t-,
C₃₋₇ cycloalkyl-CH=CH-(CH₂)_t-,
aryl-CH=CH-(CH₂)_t-,
C₁₋₆ alkylaryl-CH=CH-(CH₂)_t-,
C₁₋₆ alkyl-SO₂-(CH₂)_t-,
C₁₋₆ alkylaryl-SO₂-(CH₂)_t-,
C₁₋₆ alkoxy,
aryl C₁₋₆ alkoxy,
aryl C₁₋₆ alkyl,

contd.
A²

B1
Cont

20009YDB

(C1-6 alkyl)pamino C1-6 alkyl,
(aryl)pamino,
(aryl)pamino C1-6 alkyl,
(aryl C1-6 alkyl)pamino,
(aryl C1-6 alkyl)pamino C1-6 alkyl,
arylcarbonyloxy,
aryl C1-6 alkylcarbonyloxy,
(C1-6 alkyl)paminocarbonyloxy,
C1-8 alkylsulfonylamino,
arylcarbonylamino,
arylsulfonylamino,
C1-8 alkylsulfonylamino C1-6 alkyl,
arylsulfonylamino C1-6 alkyl,
aryl C1-6 alkylsulfonylamino,
aryl C1-6 alkylsulfonylamino C1-6 alkyl,
C1-8 alkoxycarbonylamino,
C1-8 alkoxycarbonylamino C1-8 alkyl,
aryloxycarbonylamino C1-8 alkyl,
aryl C1-8 alkoxycarbonylamino,
aryl C1-8 alkoxycarbonylamino C1-8 alkyl,
C1-8 alkylcarbonylamino C1-6 alkyl,
arylcarbonylamino C1-6 alkyl,
aryl C1-6 alkylcarbonylamino,
aryl C1-6 alkylcarbonylamino C1-6 alkyl,
aminocarbonylamino C1-6 alkyl,
arylaminocarbonylamino,
(C1-8 alkyl)paminocarbonylamino,
(C1-8 alkyl)paminocarbonylamino C1-6 alkyl,
(aryl)paminocarbonylamino C1-6 alkyl,
(aryl C1-8 alkyl)paminocarbonylamino,
(aryl C1-8 alkyl)paminocarbonylamino C1-6 alkyl,
aminosulfonylamino C1-6 alkyl,

contd.

a²

B¹
Cont

20009YDB

(C₁₋₈ alkyl)paminosulfonylamino,
(C₁₋₈ alkyl)paminosulfonylamino C₁₋₆ alkyl,
(aryl)paminosulfonylamino C₁₋₆ alkyl,
(aryl C₁₋₈ alkyl)paminosulfonylamino,
(aryl C₁₋₈ alkyl)paminosulfonylamino C₁₋₆ alkyl,
C₁₋₆ alkylsulfonyl,
C₁₋₆ alkylsulfonyl C₁₋₆ alkyl,
arylsulfonyl C₁₋₆ alkyl,
aryl C₁₋₆ alkylsulfonyl,
aryl C₁₋₆ alkylsulfonyl C₁₋₆ alkyl,
C₁₋₆ alkylcarbonyl,
C₁₋₆ alkylcarbonyl C₁₋₆ alkyl,
arylcarbonyl C₁₋₆ alkyl,
aryl C₁₋₆ alkylcarbonyl,
aryl C₁₋₆ alkylcarbonyl C₁₋₆ alkyl,
C₁₋₆ alkylthiocarbonylamino,
C₁₋₆ alkylthiocarbonylamino C₁₋₆ alkyl,
arylthiocarbonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkylthiocarbonylamino,
aryl C₁₋₆ alkylthiocarbonylamino C₁₋₆ alkyl,
(C₁₋₈ alkyl)paminocarbonyl C₁₋₆ alkyl,
(aryl)paminocarbonyl C₁₋₆ alkyl,
(aryl C₁₋₈ alkyl)paminocarbonyl,
(aryl C₁₋₈ alkyl)paminocarbonyl C₁₋₆ alkyl, and
C₇₋₂₀ polycyclyl C₀₋₈ alkylsulfonylamino,

wherein any of the alkyl groups of R⁷ and R⁸ are either unsubstituted or substituted with one to three R¹ substituents, and provided that each R⁷ and R⁸ are selected such that in the resultant compound the carbon atom to which R⁷ and R⁸ are attached is itself attached to no more than one heteroatom;

R⁹ is selected from the group consisting of
hydrogen,

contd.
a²

B1
Cont

C₁₋₈ alkyl,
aryl,
aryl C₁₋₈ alkyl,
C₁₋₈ alkylcarbonyloxy C₁₋₄ alkyl,
aryl C₁₋₈ alkylcarbonyloxy C₁₋₄ alkyl,
C₁₋₈ alkylaminocarbonylmethylene, and
C₁₋₈ dialkylaminocarbonylmethylene;

wherein

each m is independently an integer from 0 to 6;
each n is independently an integer from 0 to 6;
each p is independently an integer from 0 to 2;
each r is independently an integer from 1 to 3;
each s is independently an integer from 0 to 3; and
each t is independently an integer from 0 to 3;

and the pharmaceutically acceptable salts thereof.

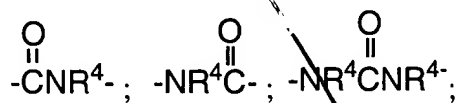
42. The compound of Claim 41 wherein Y is selected from the group consisting of

$-(CH_2)_m-$,
 $-(CH_2)_m-O-(CH_2)_n-$,
 $-(CH_2)_m-NR^4-(CH_2)_n-$,
 $-(CH_2)_m-S-(CH_2)_n-$,
 $-(CH_2)_m-SO-(CH_2)_n-$,
 $-(CH_2)_m-SO_2-(CH_2)_n-$,
 $-(CH_2)_m-O-(CH_2)_n-O-(CH_2)_p-$,
 $-(CH_2)_m-O-(CH_2)_n-NR^4-(CH_2)_p-$,
 $-(CH_2)_m-NR^4-(CH_2)_n-NR^4-(CH_2)_p-$, and
 $-(CH_2)_m-NR^4-(CH_2)_n-O-(CH_2)_p-$,

contd.
a²
B¹
Cont

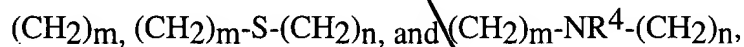
wherein any methylene (CH₂) carbon atom in Y, other than in R⁴, can be substituted by one or two R³ substituents, with the proviso that when Y is -(CH₂)_m-NR⁴-(CH₂)_n- and n = 1, then the R³ substituent on the methylene carbon in -(CH₂)_m- adjacent to the nitrogen cannot be oxo;

and Z is selected from the group consisting of



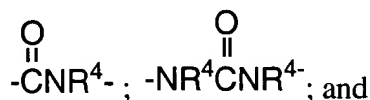
-CH₂CH₂-, and -CH=CH-, wherein either carbon atom can be substituted by one or two R³ substituents.

43. The compound of Claim 44 wherein Y is selected from the group consisting of



wherein any methylene (CH₂) carbon atom in Y, other than in R⁴, can be substituted by one or two R³ substituents, with the proviso that when Y is -(CH₂)_m-NR⁴-(CH₂)_n- and n = 1, then the R³ substituent on the methylene carbon in -(CH₂)_m- adjacent to the nitrogen cannot be oxo;

and Z is selected from the group consisting of



-CH₂CH₂-, wherein either carbon atom can be substituted by one or two R³ substituents.

44. The compound of Claim 43 wherein each R³ is independently selected from the group consisting of

hydrogen,
fluoro,

contd.
a²

trifluoromethyl,
aryl,
C₁₋₈ alkyl,
arylC₁₋₆ alkyl
hydroxyl,
oxo,
arylamino-carbonyl,
aryl C₁₋₅ alkylaminocarbonyl,
aminocarbonyl, and
aminocarbonyl C₁₋₆ alkyl;

and each R⁴ is independently selected from the group consisting of

hydrogen,
aryl,
C₃₋₈ cycloalkyl,
C₁₋₈ alkyl,
C₁₋₈ alkylcarbonyl,
arylcabonyl,
C₁₋₆ alkylsulfonyl,
arylsulfonyl,
arylC₁₋₆alkylsulfonyl,
arylC₁₋₆alkylcarbonyl,
C₁₋₈alkylaminocarbonyl,
arylC₁₋₅alkylaminocarbonyl,
arylC₁₋₈alkoxycarbonyl, and
C₁₋₈alkoxycarbonyl.

45. The compound of Claim 44 wherein R⁶, R⁷, and R⁸ are each hydrogen and R⁵ is selected from the group consisting of
hydrogen,
aryl,
C₁₋₈ alkyl,

contd.
Q 2

aryl-C \equiv C-(CH₂)_t-,
aryl C₁₋₆ alkyl,
CH₂=CH-(CH₂)_t-, and
HC \equiv C-(CH₂)_t-.

46. The compound of Claim 45 wherein R⁹ is selected from the group consisting of hydrogen, methyl, and ethyl.

47. The compound of Claim 46 wherein R⁹ is hydrogen.

48. The compound of Claim 44 wherein R⁵, R⁶, and R⁸ are each hydrogen and R⁷ is selected from the group consisting of

hydrogen,
aryl,
C₁₋₈ alkylcarbonylamino,
C₁₋₈ alkylsulfonylamino,
arylcarbonylamino,
arylsulfonylamino,
C₁₋₈ alkylsulfonylamino C₁₋₆ alkyl,
arylsulfonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkylsulfonylamino,
aryl C₁₋₆ alkylsulfonylamino C₁₋₆ alkyl,
C₁₋₈ alkoxycarbonylamino,
C₁₋₈ alkoxycarbonylamino C₁₋₈ alkyl,
aryloxycarbonylamino C₁₋₈ alkyl,
aryl C₁₋₈ alkoxycarbonylamino,
aryl C₁₋₈ alkoxycarbonylamino C₁₋₈ alkyl,
C₁₋₈ alkylcarbonylamino C₁₋₆ alkyl,
arylcarbonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkylcarbonylamino,
aryl C₁₋₆ alkylcarbonylamino C₁₋₆ alkyl,
aminocarbonylamino C₁₋₆ alkyl,

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contd.
a²

(C₁₋₈ alkyl)paminocarbonylamino,
(C₁₋₈ alkyl)paminocarbonylamino C₁₋₆ alkyl,
(aryl)paminocarbonylamino C₁₋₆ alkyl,
arylaminocarbonylamino,
(aryl C₁₋₈ alkyl)paminocarbonylamino,
(aryl C₁₋₈ alkyl)paminocarbonylamino C₁₋₆ alkyl,
aminosulfonylamino C₁₋₆ alkyl,
(C₁₋₈ alkyl)paminosulfonylamino,
(C₁₋₈ alkyl)paminosulfonylamino C₁₋₆ alkyl,
(aryl)paminosulfonylamino C₁₋₆ alkyl,
(aryl C₁₋₈ alkyl)paminosulfonylamino,
(aryl C₁₋₈ alkyl)paminosulfonylamino C₁₋₆ alkyl,
C₁₋₆ alkylthiocarbonylamino,
C₁₋₆ alkylthiocarbonylamino C₁₋₆ alkyl,
arylthiocarbonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkylthiocarbonylamino,
aryl C₁₋₆ alkylthiocarbonylamino C₁₋₆ alkyl, and
C₇₋₂₀ polycyclyl C₀₋₈ alkylsulfonylamino.

49. The compound of Claim 48 wherein R⁵, R⁶, and R⁸ are each hydrogen and R⁷ is selected from the group consisting of

hydrogen,
aryl,
C₁₋₈ alkylcarbonylamino,
aryl C₁₋₆ alkylcarbonylamino,
arylcarbonylamino,
C₁₋₈ alkylsulfonylamino,
aryl C₁₋₆ alkylsulfonylamino,
arylsulfonylamino,
C₁₋₈ alkoxycarbonylamino,
aryl C₁₋₈ alkoxycarbonylamino,
arylaminocarbonylamino,

contd.
a²

(C₁₋₈ alkyl)_paminocarbonylamino,
(aryl C₁₋₈ alkyl)_paminocarbonylamino,
(C₁₋₈ alkyl)_paminosulfonylamino, and
(aryl C₁₋₈ alkyl)_paminosulfonylamino.

50. The compound according to Claim 49 wherein R⁹ is selected from the group consisting of hydrogen, methyl, and ethyl.

51. The compound according to Claim 50 wherein R⁹ is hydrogen.

52. The compound of Claim 44 which is:

3-[5-(2-Amino-pyrimidin-4-yl)-pentanoylamino]-3(S)-(quinolin-3-yl)-propionic acid;

and the pharmaceutically acceptable salts thereof.

53. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 41 and a pharmaceutically acceptable carrier.

54. The composition of Claim 53 which further comprises an active ingredient selected from the group consisting of

- a) an organic bisphosphonate or a pharmaceutically acceptable salt or ester thereof,
- b) an estrogen receptor modulator,
- c) a cytotoxic/antiproliferative agent,
- d) a matrix metalloproteinase inhibitor,
- e) an inhibitor of epidermal-derived, fibroblast-derived, or platelet-derived growth factors,
- f) an inhibitor of VEGF,
- g) an inhibitor of Flk-1/KDR, Flt-1, Tck/Tie-2, or Tie-1,
- h) a cathepsin K inhibitor, and
- i) a farnesyl transferase inhibitor or a geranylgeranyl transferase inhibitor or a dual farnesyl/geranylgeranyl transferase inhibitor;

contd
Q²

and mixtures thereof.

55. The composition of Claim 54 wherein said active ingredient is selected from the group consisting of

- a) an organic bisphosphonate or a pharmaceutically acceptable salt or ester thereof,
- b) an estrogen receptor modulator, and
- c) a cathepsin K inhibitor;
and mixtures thereof.

56. The composition of Claim 55 wherein said organic bisphosphonate or pharmaceutically acceptable salt or ester thereof is alendronate monosodium trihydrate.

57. The composition of Claim 54 wherein said active ingredient is selected from the group consisting of

- a) a cytotoxic/antiproliferative agent,
- b) a matrix metalloproteinase inhibitor,
- c) an inhibitor of epidermal-derived, fibroblast-derived, or platelet-derived growth factors,
- d) an inhibitor of VEGF,
- e) an inhibitor of Flk-1/KDR, Flt-1, Tck/Tie-2, or Tie-1, and
- f) a cathepsin K inhibitor;
and mixtures thereof.

58. A method of eliciting an integrin receptor antagonizing effect in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 41.

59. The method of Claim 58 wherein the integrin receptor antagonizing effect is an $\alpha v\beta 3$ antagonizing effect.